

Amendment To The Claims

1. (Currently Amended) A method for screening for agents that affect protein degradation rates, the method comprising:

i) expressing a different fusion protein in each cell within a library of cells, the fusion protein comprising a reporter protein and a protein encoded by a sequence from a cDNA library derived from a sample of cells, the sequence from the cDNA library varying within the cell library;

ii) inhibiting further expression of the fusion protein to allow the expressed fusion protein to degrade in the cell;

iii) selecting a population of cells from the library of cells based on the population of cells having different reporter signal intensities than other cells in the library, the difference being indicative of the population of cells expressing shorter lived fusion proteins than the fusion proteins expressed by the other cells in the library;

iv) contacting the selected population of cells from step iii) with a plurality of agents which may affect protein degradation rates;

v) for each agent, selecting cells in the selected population from step iv) based on whether the cells have different reporter signal intensities than the cells in the selected population of cells from step iii) without being contacted with the agent, the difference being indicative of the selected cells expressing short lived fusion proteins whose degradation is affected by the agent; and

vi) characterizing the fusion proteins expressed by the selected cells for each agent.

2. (Currently Amended) A method according to claim 1, ~~wherein the method further comprises~~ further comprising:

comparing which fusion proteins are expressed by the selected cells for each agent.

3. (Currently Amended) A method for monitoring effects different growth conditions have on expression of short-lived proteins, the method comprising:

exposing samples of cells to different growth conditions;

forming cDNA libraries from the sample of cells after exposure to the different growth conditions;

forming a library of cells for each cDNA library, the cells in the library expressing a different fusion protein comprising a reporter protein and a protein encoded by a sequence from the cDNA library derived from a sample of cells, the sequence from the cDNA library varying within the cell library;

for each library of cells,

inhibiting further expression of the fusion protein to allow the expressed fusion protein to degrade in the cell,

identifying cells within the library that express fusion proteins that are degraded *in vivo* more rapidly than other fusion proteins, and

characterizing fusion proteins expressed by the identified cells; and

comparing which fusion proteins are characterized for each library of cells, differences in the characterized fusion proteins indicating differences in the short-lived proteins expressed by when the cells are exposed to the different growth conditions.

4. (Original) A method according to claim 3, wherein exposing the samples of cells to different conditions comprises exposing the cells to different agents.

5. (Previously Presented) A method according to claim 3, wherein identifying cells within the library that express fusion proteins that are degraded *in vivo* more rapidly than other fusion proteins comprises

selecting a population of the cells based on whether the cells have different reporter signal intensities than other cells after the rate of protein expression or degradation has been modified, the difference being indicative of the selected population of cells expressing shorter lived fusion proteins than the fusion proteins expressed by the other cells in the library.

6. (Currently Amended) A method for monitoring effects different growth conditions have on expression of short-lived proteins, the method comprising:

exposing samples of cells to different conditions;

forming cDNA libraries from the sample of cells after exposure to the different growth conditions;

forming a library of cells for each cDNA library, each cell in the library expressing a different fusion protein comprising a reporter protein and a protein encoded by a sequence from the cDNA library derived from a sample of cells, the sequence from the cDNA library varying within the cell library;

for each library of cells,

partitioning the library of cells into populations of cells based on an intensity of a reporter signal from the fusion protein such that cells partitioned into a given population have a reporter signal within a desired range of reporter signal intensity,

expressing the fusion proteins in the given population of cells,

inhibiting further expression of the fusion protein in the given population of cells to allow the expressed fusion protein to degrade in the cell;

selecting a subpopulation of the cells from the given population of cells based on whether the cells have a different reporter signal intensity than the other cells in the given population, the difference being indicative of the selected subpopulation of cells expressing shorter lived fusion proteins than the fusion proteins expressed by the other cells in the given population,

characterizing fusion proteins expressed by at least a portion of the selected cells; and

comparing which fusion proteins are characterized for each library of cells,

differences in the characterized fusion proteins indicating differences in the short-lived proteins expressed by when the cells are exposed to the different ~~different~~ growth conditions.

7. (Original) A method according to claim 6 wherein exposing the samples of cells to different conditions comprises exposing the cells to different agents.

8. (Currently Amended) A method for screening for differences in short-lived proteins expressed by first and second cell samples, the method comprising:

forming cDNA libraries for first and second samples of cells;

forming a library of cells for each cDNA library, the cells in the library expressing a different fusion protein comprising a reporter protein and a protein encoded by a sequence from the cDNA

library derived from a sample of cells, the sequence from the cDNA library varying within the cell library;

for each library of cells,

inhibiting further expression of the fusion protein to allow the expressed fusion protein to degrade in the cell,

identifying cells within the library that express fusion proteins that are degraded *in vivo* more rapidly than other fusion proteins, and

characterizing fusion proteins expressed by the identified cells; and

comparing which fusion proteins are characterized for each library of cells, differences in the characterized fusion proteins indicating differences in the short-lived proteins expressed by the first and second samples cells.

9. (Currently Amended) A method for screening for differences in short-lived proteins expressed by first and second cell samples, the method comprising:

forming cDNA libraries for first and second samples of cells;

forming a library of cells for each cDNA library, the cells in the library expressing a different fusion protein comprising a reporter protein and a protein encoded by a sequence from the cDNA library derived from a sample of cells, the sequence from the cDNA library varying within the cell library;

for each library of cells,

partitioning the library of cells into populations of cells based on an intensity of a reporter signal from the fusion protein such that cells partitioned into a given population have a reporter signal within a desired range of reporter signal intensity,

expressing the fusion proteins in the given population of cells,

inhibiting further expression of the fusion protein in the given population of cells to allow the expressed fusion protein to degrade in the cell;

selecting a subpopulation of the cells based on whether the cells have different reporter signal intensities than the other cells after the rate of protein expression or degradation has been modified, the difference being indicative of the selected

subpopulation of cells expressing shorter lived fusion proteins than the fusion proteins expressed by the other cells in the given population, and
characterizing fusion proteins expressed by at least a portion of the selected cells; and
comparing which fusion proteins are characterized for each library of cells, differences in the characterized fusion proteins indicating differences in the short-lived proteins expressed by the first and second samples cells.

10. (Previously Presented) A method according to claim 1, wherein inhibiting further expression of the fusion protein includes inhibiting further synthesis of the fusion protein.

11. (Previously Presented) A method according to claim 10, wherein the further synthesis of the fusion protein is inhibited by adding cycloheximide to the cell.

12. (Previously Presented) A method according to claim 1, wherein the reporter protein is a fluorescent protein.

13. (Previously Presented) A method according to claim 1, wherein the reporter protein is a green fluorescence protein (GFP) or enhanced green fluorescence protein (EGFP).

14. (Previously Presented) A method according to claim 8, wherein inhibiting further expression of the fusion protein includes inhibiting further synthesis of the fusion protein.

15. (Previously Presented) A method according to claim 14, wherein the further synthesis of the fusion protein is inhibited by adding cycloheximide to the cell.

16. (Previously Presented) A method according to claim 8, wherein the reporter protein is a fluorescent protein.

17. (Previously Presented) A method according to claim 8, wherein the reporter protein is a green fluorescence protein (GFP) or enhanced green fluorescence protein (EGFP).